REMARKS/ARGUMENTS

The Pending Claims

Claims 77-91 are pending and are directed to a screening method for a somatic cell nuclear reprogramming substance.

Amendments to the Claims

The claims have been amended to point out more particularly and claim more distinctly the invention. Claims 15, 16, 22, and 71-76 have been canceled. New claims 77-91 have been added and are supported by original claims 7, 8, and 10, and the specification at, for example, Table 1 and page 5, line 36, through page 8, line 13. No new matter has been added by way of these amendments to the claims.

Summary of the Office Action

The Office has rejected claims 15, 16, and 71-76 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement.

The Office has rejected claims 15 and 16 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite.

The Office has rejected claims 15, 16, 22, and 71-76 under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent Application Publication 2008/0280362 (Jaenisch et al.).

Reconsideration of these rejections is hereby requested.

Discussion of the Enablement Rejection

The Office contends that claims 15, 16, and 71-76 lack enablement. In particular, the Office contends that the specification does not provide enablement for isolated cells other than fibroblasts containing a drug resistance gene inserted into an ECAT4 gene. The Office contends that it was known at the time of filing that cells must undergo more than 45 divisions for selection and that the only somatic cells that are capable of undergoing the

required number of passages without senescing are fibroblasts. The Office also contends that the claims encompass somatic cells isolated from knock-in animals with a drug resistance gene inserted into both copies of ECAT4, but if both ECAT4 genes were absent and functional ECAT4 was not supplied, the embryos would not develop.

Claims 15, 16, and 71-76 have been canceled, thereby rendering the enablement rejection moot. Applicants believe that the subject matter of new claims 77-91 is sufficiently enabled for the reasons discussed below.

New claims 77-91 are directed to methods of screening for a somatic cell nuclear reprogramming substance, which comprises (a) a step for providing an isolated somatic cell comprising a marker gene operably linked to the expression control region of the ECAT2 gene and/or a marker gene operably linked to the expression control region of the ECAT3 gene, (b) a step for bringing into contact a test substance with the somatic cell of the aforementioned step (a), (c) a step following the aforementioned step (b), for detecting the presence or absence of the emergence of cells expressing the marker gene(s), and (d) a step for selecting a test substance that allows the emergence of the cells as a candidate somatic cell nuclear reprogramming substance.

The pending claims encompass the random insertion of a marker gene under the control of an exogenous ECAT2 and/or a marker gene under the control of an exogenous ECAT3 gene. Random insertion of a transgene into the genome of somatic cells can be accomplished by direct transfer of the marker gene to the somatic cells or, in the case of non-human animals, via a transgenic animal. When the marker gene is targeted to the endogenous ECAT2 and/or ECAT3 gene, the somatic cells preferably are mouse cells (see claims 78, 83, and 88). Mouse somatic cells that comprise the marker gene(s) under the control of the endogenous ECAT2 and/or ECAT3 gene can be obtained by introducing a targeting vector into mouse ES cells, selecting an ES cell expressing the marker gene, transplanting the selected ES cell into a mouse to produce a chimeric mouse in which the ES cell contributes to the germline, obtaining offspring mice in which the marker gene(s) is(are) knocked-in the ECAT2 and/or ECAT3 gene, and isolating the desired somatic cells from the mice.

Once the somatic cells comprising the marker gene(s) under the control of ECAT2 and/or ECAT3 are obtained, the cells are screened for a nuclear reprogramming substance by bringing the cells into contact with a test substance. If the test substance is a nuclear reprogramming substance, the cells will produce the marker gene product and survive selection. The somatic cells that are contacted with a test substance that is a nuclear reprogramming substance will be reprogrammed to pluripotent stem cells capable of indefinitely proliferating. Therefore, even if the starting somatic cells are not capable of numerous divisions (e.g., 45 divisions as noted by the Office), the administration of a nuclear reprogramming substance to the somatic cells will result in reprogramming of the somatic cells to pluripotent stem cells that are capable of achieving numerous divisions. For instance, Example 1 (see pages 71-73 of the specification) and Example 3 (see pages 74-76 of the specification) describe the use of lymphocytes as the starting somatic cells. Accordingly, the somatic cells for use in the inventive methods are not limited to fibroblasts as indicated by the Office.

Both the ECAT2 and ECAT3 gene products are specifically expressed in ES cells, testis, and ovaries (see, e.g., page 76, lines 2-4, of the specification). This indicates that a cell expressing a marker gene(s) under the control of the ECAT2 and/or ECAT3 gene is an ES cell irrespective of the roles of ECAT2 and ECAT3 in an ES cell. Example 3 (see pages 74-76 of the specification) clearly demonstrates that ECAT2-reporter somatic cells can detect reprogramming of lymphocytes to pluripotent stem cells equivalent to ES cells. Example 1 (see pages 71-73 of the specification) demonstrates that ECAT3-reporter somatic cells can detect the same. Even if one were to assume that all of the ECAT2-expressing cells are not ES cells, all ES cells can be detected by the claimed method, for example, by detecting the expression of other ECAT genes.

Furthermore, regarding the Office's concern that the claims encompass the insertion of marker genes into both copies of the ECAT gene, Applicants note that the ECAT2 and ECAT3 gene products are not essential for the maintenance and growth of ES cells (see, e.g., page 76, lines 4-5, of the specification). Therefore, a marker gene can be inserted into either

or both of the ECAT2 and ECAT3 genes (see claims 80, 85, and 90) without risk that an embryo will not develop.

For the above-described reasons, Applicants believe that one of ordinary skill in the art would understand how to practice the invention with a reasonable expectation of success given the teachings in the specification.

Discussion of the Indefiniteness Rejection

The Office contends that claims 15, 16, and 22 are unclear. Applicants note that these claims have been canceled, thereby rendering the indefiniteness rejection moot. Applicants believe that the pending claims are sufficiently clear.

Discussion of the Section 102(e) Rejection

The Office contends that claims 15, 16, 22, and 71-76 are anticipated by the Jaenisch reference, which reference allegedly discloses an *in vitro* assay for determining compounds that affect the expression of pluripotency genes, such as Nanog (ECAT4), where a transgenic cell comprising a selectable marker gene, such as an antibiotic resistance gene, is treated with an agent.

As discussed above, claims 15, 16, 22, and 71-76 have been canceled in an effort to advance prosecution, thereby rendering moot the anticipation rejection.

New claims 77-91 recite subject matter similar to the subject matter of original claims 7, 8, and 10, which the Office indicated were free of the prior art in the Office Action dated February 17, 2010. Therefore, Applicants believe that the subject matter of the pending claims is not anticipated or obvious in view of the prior art.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the

prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

John Kilyk, Jr. , Reg. No. 30,763
LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite 4900
180 North Stetson Avenue
Chicago, Illinois 60601-6731
(312) 616-5600 (telephone)
(312) 616-5700 (facsimile)

Date: October 4, 2010